REMARKS

Applicants respectfully request reconsideration of the present application in view of the amendments to the claims and the foregoing reasons.

Pending Claims

Claims 1 and 4-23, 25-28, and 30-74 are requested to be canceled without prejudice or disclaimer to pursuing such claims in a separate application. Claims 24 and 29 were previously canceled.

Claim 2 has been amended to incorporate the limitations of now canceled claim 1.

Claims 75-112 are new. These claims are directed to vaccine compositions and methods of their use and find support in the prior compound and method claims but with the compound claims now rewritten in their composition forms. Claims 75-107 are dependent on claim 2 or on claims dependent on claim 2. Claim 108 is an independent claim directed to vaccine compositions comprising the specific compounds disclosed in the application, with claims 109 and 110 dependent on claim 108. Specific correspondence of the new claims is as follows:

New claims 75-82 correspond to original claims 32-39.

New claim 83 corresponds to previously presented claim 40.

New claims 84-92 correspond to original claims 41-49.

New claim 93 corresponds to previously presented claim 50.

New claims 94-107 correspond to original claims 51-64.

New claim 109 corresponds to previously presented claim 74. The compounds of claim 109 are listed in Table 1. Pyridine-2-carbaldehyde thiosemicarbazone recited in claim 110 is compound 113, the first compound in Table 2.

New claims 111-112 correspond to the original method claims 70-71, now made dependent on claims 2 and 108.

Applicants wish to correct a previous unintentional misstatement on the Applicants' part that pyridine-2-carbaldehyde thiosemicarbazone is a compound of formula IX of claim 63. While compounds of formula IX are also compounds of formula I in claim 2, pyridine-2-carbaldehyde thiosemicarbazone is only a compound of formula I.

No new matter has been added by the amendments.

Upon entry of the amendments, claims 2-3 and 75-112 are pending.

Claim Objections

The 35 U.S.C. §102 rejection

Claim 1 stands rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Gall. In the interest of expediting prosecution, Applicants have canceled Claim 1. Withdrawal of this rejection is respectfully requested.

The 35 U.S.C. §103 rejection

Claims 1-3 and 63 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Gall in view of Blanz, *et al.* Claims 1 and 63 have been canceled by this amendment. The rejection and its supporting remarks are respectfully traversed as applied to the pending claims.

The Office states that:

> The claims are drawn to a vaccine/adjuvant composition comprising, in part, a thiosemicarbazone or derivative thereof serving as the adjuvant. Gall teaches the uses of many substances useful as adjuvants to enhance the immunogenicity of vaccines. **Gall specifically teaches the use of several thiosemicarbazones that enhanced the immunogenicity of diphtheria toxoid in guinea-pigs (see Table 7, p. 380)**. Gall doesn't teach the use of pyridine-2-carbaldehyde thiosemicarbazone or other members of the class of thiosemicarbazones characterized by formula IX of Claim 63. Blanz, et al. specifically teaches the use of pyridine-2-carbaldehyde thiosemicarbazone as an anticancer therapeutic.
>
> It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the vaccine/adjuvant composition of Gall by substituting pyridine-2-carbaldehyde thiosemicarbazone for one of the thiosemicarbazones. The skilled artisan would have been motivated to do so because of the high solubility of pyridine-2-carbaldehyde thiosemicarbazone, as taught by Blanz, et al. **There would be a reasonable expectation of success, given the general utility of thiosemicarbazones, as taught by Gall.** Thus the invention of claims 1-3 and 63 was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made. (***emphasis added in bold***)

Applicants respectfully point out that the Office has not established a *prima facie* case of obviousness.

First, the combination of Gall and Blanz, et al does not teach the claim limitation of an effective amount of a vaccine adjuvant to potentiate the cell-mediated immune response to the vaccine. The Gall compounds were tested at a specific concentration, and Gall taught away from testing at higher concentrations, noting on page 370 that:

> After some preliminary investigations, in which substances were tested in doses of 10 μg, 500 μg, or 1 mg or over a range of doses, the dose of adjuvant was fixed at 100 μg. For most substances this appeared to be enough to produce substantial adjuvant activity if any was to be forthcoming, and in those substances in which the dose relationship were more carefully studied it was found that if there was activity at this level, increasing the quantity of adjuvant did not materially alter the order of response. There are some exceptions to this rule (notably amongst the silicas), and not doubt some activities have been missed through using too low a does, but in general this seems unlikely to apply to the type of compound under consideration here.

Secondly, Gall does not teach the use of thiosemicarbazones as adjuvants as is alleged. Gall states on page 381 in reference to Table 7 that:

> None of the thioureas, thiosemicarbazides or thiosemicarbazones showed adjuvant activity, whether or not a long alkyl chain was present. These compounds, bearing the =S group, are neutral or near neutral.

The teachings of Gall therefore teaches away from the use of the thiosemicarbazones as adjuvants. Absent teachings to the contrary, there exist no motivation for one of skill in the art to substitute the inactive thiosemicarbazone adjuvants of Gall with the thiosemicarbazones of Blanz with the expectation that the compounds of Blanz can act as adjuvants.

Withdrawal of the rejection of claims 2 and 3 under 35 U.S.C. §103 and examination of new claims 75-112 is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid

amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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